

CALIFORNIA INSTITUTE OF TECHNOLOGY  
PASADENA

DIVISION OF BIOLOGY  
KERCKHOFF LABORATORIES OF BIOLOGY

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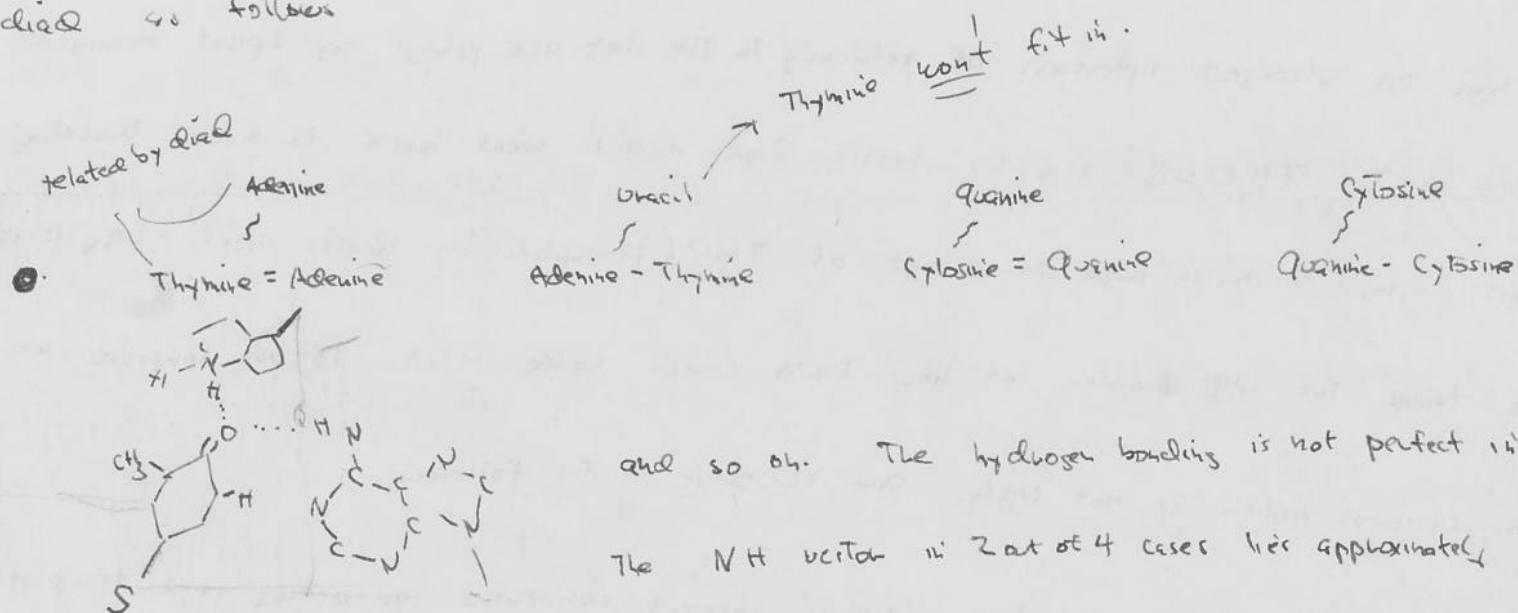
Dear Francis

I have meant to reply sooner but have been rather preoccupied with work. Though I had the strongest intentions of returning to the lab one phase, my spirit remained with RNA and the TIECLUB and so Leslie Orgel and I went back to model building. After first trying to make more sense out of TMV (prompted by Rosies visit - very amiable!) we tried the old problem of how DNA could make RNA. To our surprise we have an answer which is not ugly. Our reasoning is the following.

DNA could make RNA by either chemical conversion or acting as a template. The former is ruled out by isotope experiments and so we have to decide whether the two strands of DNA are active. If a one strand stage operates it likely does it by a DNA like base pairing mechanism. The answer in this case is trivial, even if it proved possible to stick a RNA strand in a two stranded structure. Of this I'm sceptical. Moreover, I don't like the idea of the two strands having to separate since we have no reason to believe it would be stable. Still more I can't see an easy answer of why ribonucleotides & deoxy nucleotides wouldn't occasionally get mixed up and thus cause mistakes in the replication process.

We therefore consider it likely that the two stranded helix is the functional least. For an attractive force only hydrogen bonds need be considered since

van der Waals forces would not distinguish Adenine from Guanine with the required accuracy. Likewise Uracil from Cytosine. Two types can be formed  $\text{NH}\cdots\text{O}$  and  $\text{NH}\cdots\text{N}$ . The latter is too weak if used only  $\approx$  3-4 helix and so the  $\text{NH}\cdots\text{O}$  bond must be employed. The requirement is that the 4 base pairs yield 4 specific holes in such a way that a regular backbone is of RNA can be formed. We have found only one arrangement which works. It employs a II diad as follows

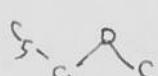


and so on. The hydrogen bonding is not perfect in that the NH vector in 2 out of 4 cases lies approximately  $20^\circ$  from the CN...O angle of  $120^\circ$ . However Pauling

said the other chemists are not bothered. The bond is still strong enough to be useful. In this way we define exactly the backbone arrangement of the third RNA chain. Its direction is  $\approx 15^\circ$ . At first site this seems nasty especially as the glucosidic angle does not point toward the center. In fact I don't think it can be built even by cheating with its radius. The main difficulty is the OH groups of the sugar. This problem

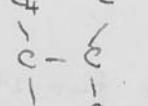
can be resolved by eliminating it to form the cyclic anhydride. When this is

done, a very very pretty



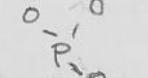
helix results in which everything fits

nicely. It of course will be



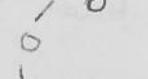
unstable but this shouldn't bother us as we

need a device to remove the



RNA once formed from its DNA. That is

we postulate its anhydride



to decompose to yield normal RNA

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The scheme is completely hypothetical but yet at the same time structurally possible.  
I don't have the coordinates yet for the 3D chain but I know that this will not be  
an obstacle as there are no bad contacts at all.

It is likely that we shall write up the structure immediately and submit it to the  
Proceedings of the National Academy. Of course it may be wrong but at least it's a

try to find a template in DUT and until a better one comes along, it's useful to

consider. As soon as we get a MS, I'll send it to you for comments. The writing should  
take about 2 weeks.

I was in Woods Hole during "Edna" - rather fun - Szent Gyorgyi cottage was  
blown to pieces during "Carol" and "Edna" blew the pieces still further away.

Regards to Odile, John, Max, etc

Jim

P.S. The first RNA TIE has been woven. More on order

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